Effect of magnesium sulfate seizure prophylaxis on fetal myocardial performance index in severe preeclampsia and eclampsia

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Abstract

Objective: This study aimed to investigate the effect of magnesium sulfate treatment on fetal cardiac function during seizure prophylaxis of pregnant women diagnosed with severe preeclampsia and eclampsia. Fetal cardiac function was evaluated with the modified myocardial performance index (mod-MPI) before and after prophylaxis. **Methods:** A total of 50 pregnant women diagnosed with severe preeclampsia or eclampsia were involved. The characteristics of the participants, medical and obstetric history, ultrasound and laboratory findings were recorded. Fetal mod-MPI was obtained before and after magnesium treatment. Data were analyzed with appropriate statistical tests and $p < 0.05$ was considered to indicate statistical significance . **Results:** The mean maternal and gestational ages of pregnant women were 31.7 ± 5.9 and 32.4 ± 4.5. Mean mod-MPI before and after prophylaxis were 0.41 ± 0.18 and 0.49 ± 0.09, respectively ($p<0.05$). **Conclusion:** There was a significant increase in fetal mod-MPI after magnesium prophylaxis was given to severe preeclampctic/eclamptic women. The higher the mod-MPI, the worse the fetal cardiac function. This might have been the result of magnesium leading to an increased isovolumetric relaxation time. **Key words:** Preeclampsia, magnesium sulfate, myocardial performance index, eclampsia, fetus

Introduction

Preeclampsia accompanies 2% of pregnancies, and is an important cause of perinatal and maternal morbidity and mortality [1,2] . Preeclampsia is diagnosed when novel onset of hypertension and proteinurea or end-organ damage occurs after 20 weeks of gestation [3] . Eclampsia is diagnosed after seizures without other etiologies are observed in a preeclamptic pregnancy [4] .

In order to prevent seizure, magnesium sulfate prophylaxis is used as a first-choice treatment. It prevents further seizures in eclampsia and any future seizures in preeclampsia [5-7] . When compared with placebo, magnesium sulfate decreases the risk of deterioration from preeclampsia to eclampsia by 60% [8] . Besides prevention of seizures, magnesium sulfate is a systemic vasodilator that elongates sinoatrial impulse production and conduction period [9,10] . Given the cardiovascular effects, magnesium sulfate may affect fetal cardiac function [11] .

The myocardial performance index (MPI) was used by Tei et al in the evaluation of cardiac functions in adult cardiomyopathy. Being a non-invasive method derived from Doppler ultrasound, MPI is useful as a global index of myocardial function. MPI is derived by dividing the sum of the isovolumetric contraction time (ICT) and the isovolumetric relaxation time (IRT) by the ejection time (ET) [12] . Tsutsumi et al. were the first to use MPI to assess fetal cardiac function [13] . Subsequently, Hernandez-Andrade et al. utilized aortic and mitral valve closure and opening clicks on Doppler ultrasound and described the modified MPI (Mod-MPI). This modification increased interobserver and intraobserver reproducibility and reliability [14,15] .

There are studies that have investigated preeclampsia and fetal cardiac function by MPI but they did not find any significant difference [16,17]. However, there is no previous study that aimed to evaluate the effect of magnesium sulfate prophylaxis used for prevention of seizures in preeclamptic/eclamptic pregnant women on fetal cardiac function. Therefore, this study was designed to assess the effect of magnesium sulfate seizure prophylaxis on fetal cardiac function using Mod-MPI.

Methods

Ethical approval

This study was presented to and approved by the Ethical Committee of Van Yuzuncu Yil University (Date: 06.12.2019- Approval No. 11). The study was designed in accordance with the ethical standards of the Declaration of Helsinki. The study participants were briefed about the study and informed consent was obtained.

Study population

This prospective cohort study involved 50 singleton pregnant women diagnosed with severe preeclampsia or eclampsia who received seizure prophylaxis with magnesium sulfate before delivery. The participants had ages between 18 and 45 years old and were hospitalized at the Obstetrics Clinics of Van Yuzuncu Yil University between April 2021 and April 2022. Severe preeclampsia was diagnosed after 20th weeks of gestation if any of two conditions were observed: Blood pressure (BP) equal to or higher than 160 mm Hg for systolic BP or 110 mm Hg for diastolic BP, proteinurea greater than 300 mg/day, creatinine greater than 1.1 mg/dL or a two-fold increase in basal creatinine levels, a two-fold increase in liver function tests, severe and new onset central nervous system signs such as blurred vision and severe headaches, platelet count less than 100,000/mL or presence of pulmonary edema. Eclamptic patients were diagnosed if a seizure was observed in a preeclamptic woman with no other explanation for the seizures. These diagnoses were made complying with ACOG criteria [3]. Pregnant women with acute kidney disease (creatinine higher than 2.5 mg/dL) or having a fetus with cardiac defects or growth retardation were excluded from the study. The patient characteristics (age, height, weight, comorbidities, prescriptions including antihypertensive treatment, obstetric history), laboratory and ultrasonographic calculations (fetal biometric measurements, fetal umbilical and heart Doppler), maternal serum magnesium levels and obstetric outcomes (delivery mode, APGAR scores, etc.) were recorded.

Magnesium sulfate seizure prophylaxis and ultrasonographic evaluation

Magnesium sulfate prophylaxis was applied intravenously at 4.5 grams as loading dose and at 2 grams/hour continuous dose. Maternal serum and fetal mod- MPI calculations were obtained just before the seizure prophylaxis was given and at the second hour after the prophylaxis.

Mod-MPI measurement was done by a perinatologist experienced in mod-MPI calculation, fetal echocardiography and Doppler ultrasonography. Voluson E6 (GE Medical Systems, Waukesha, WI, USA) and a curvilinear probe of 6-9 MHz was utilized in ultrasonographic evaluation of the fetal heart when the fetus was still and the fetal heart was apical. The Doppler sample size was opened at 3-5 mm and placed on the lateral wall of the ascending aorta covering both mitral and aortic valves [18]. Ultrasonographic examination complied with the instructions of the International Society of Ultrasound and Obstetrics and Gynecology (ISUOG) Practice Guidelines [19]. Modified MPI measurement was done using the left ventricle and as described by Hernandez-Andrade et al [14,15]. The insonation angle was between 0 and 15 degrees. Doppler gain was adjusted for clear appearance of valve clicks, sweep velocity was 5 cm/s and wall motion filter was 300 Hz. The period between mitral valve closure and opening of the aortic valve was the isovolumetric contraction time (ICT). The isovolumetric relaxation time (IRT) was described as the period between aortic valve closure and opening of the MV. Ejection time (ET) was the period between opening and closure of the aortic valve. The formula (ICT+IRT)/ET was used for the mod-MPI calculation [12].

Statistical Analysis

Data were analyzed using IBM SPSS Statistics 21.0. Categorical variables were represented as number and percentage, continuous numerical variables were represented as mean, standard deviation, minimum and maximum values. Distribution analysis was done by the Shapiro-Wilk method. Parametric data were compared with Spearman correlation test and nonparametric data with Wilcoxon test. $p < 0.05$ was considered to indicate statistical significance.

Results

The characteristics of the pregnant women are given in Table 1. Sixty-eight percent of women had comorbidities. The major comorbidity was gestational diabetes and hypothyroidism (26% and 22% of women, respectively). Ten percent of women had pregestational hypertension. The other comorbidities were coronary artery disease and chronic kidney disease. All of the women were on antihypertensive medication. Laboratory work-up of the pregnants are shown in Table 2.

Ultrasound finding of the fetuses and gestationa age are given in Table 3. Mean umbilical artery systolic/diastolic ratio, umbilical artery pulsatility index and median cerebral artery pulsatility index were 3.1 ± 1.05, 1.18 ± 0.16 and 1.32 ± 0.13, respectively.

Eighty-two percent of the women had a Cesarean section. The mean APGAR scores at one and five minutes were 6.1 and 7.9, respectively.

The magnesium serum levels before and after magnesium sulfate prophylaxis are shown in Table 4. The increase in magnesium serum levels after seizure prophylaxis was 2.6 mg/dL and 0.07 in MPI (Figure 1).

There were no correlations between MPI difference and age, BMI, gravida, parity, abortus, hemoglobin, thrombocyte count, white blood cell count, liver function tests, creatinine, fibrinogen, INR, gestational week, biparietal diameter, head circumference, abdominal circumference, femur length, umbilical artery SD, PI, RI, middle cerebellar artery peak systolic velocity, APGAR scores, or serum magnesium level difference.

Conclusions

To our knowledge, this is the first study investigating the effect of neuroprotective magnesium sulfate therapy on fetal mod-MPI regarding fetal cardiac function.

Neonatal mild myocardial injury and cardiac dysfunction of babies of preeclamptic mothers has been shown previously [20]. Therefore, cardiovascular risks of neonates from preeclamptic women might begin in utero. Acknowledging this, the effects of magnesium sulfate therapy on the fetal heart are unknown. This study showed that there was a significant increase in mod-MPI after magnesium sulphate therapy. Promket et al. showed that fetuses of preeclamptic women and of healthy pregnancies did not differ in mod-MPI and that the mean mod-MPI was 0.44 ± 0.11. Api et al. compared mod-MPI of severe preeclampsia, mild preeclampsia and normotensive pregnant women fetuses and found that they also did not differ in mod-MPI (severe preeclamptic women fetuses had a mean mod-MPI of 0.44 ± 0.06) [17]. Our study results were similar to these studies. When our mod-MPI results were evaluated with reference mod-MPI measurements, it seems that reference values have a wide range. Falkensammer et al. declared left heart mod-MPI as a constant value of 0.4 whereas Eidem et al. found it to be 0.35 [21,22]. Friedman et al reported 0.53 [23]. In addition, Hernandez-Andrade et al. found a slight increase in mod-MPI from 19 to 39 weeks of gestation, as 0.35 and 0.37, respectively. According to Hernandez-Andrade et al., the 5^{th}, 50^{th} and 95^{th}percentile of mod-MPI for the mean gestational age of our study group would be 0.29-0.37-0.44, respectively [15]. The mean mod-MPI of our study (0.41 ± 0.18) lies between the 50^{th} and 90^{th} percentiles.

The initial fetal mod-MPI mean in this study is compatible with the literature. However, magnesium sulfate therapy increased the fetal mod-MPI to above reference ranges. This might indicate an adverse effect of magnesium sulfate therapy on fetal cardiac function.

Magnesium effects on MPI, effect of timing of therapy and how isovolumetric contraction time is affected are unknown. Magnesium is known as a strong vasodilatator that does not increase cardiac output but increases stroke volume and decreases sinus rate and thus has antiarrythmic effects. Nakaigiwa et al. showed that elongation of isovolumetric relaxation time is directly proportional to magnesium dose. As isovolumetric relaxation time is directly proportional to mod-MPI, the increase might be an effect of increased isovolumetric relaxation time. The important point is the adverse effect on mod-MPI and therefore adversely affected cardiac function, which is added to the adverse effects of being a newborn of a preeclamptic mother. This finding may not be clinically important but we suggest this should be taken into consideration.

The study results were compared with the literature, there could not be a control group comparison since without an indication, magnesium therapy cannot be given to uncomplicated pregnancies beyond the 32nd gestational age. In addition, all of the pregnant women were on antihypertensive therapy. There is no known evidence regarding the synergetic or antagonistic effect of antihypertensive medication with magnesium on fetal cardiac function. Future studies might investigate magnesium effects on fetal mod-MPI only used in neuroprophylaxis. Furthermore, the mean maternal magnesium level of pregnant women in this study was lower than the target level range of plasma magnesium known to prevent eclampsia. Future studies might use a loading dose of 6 gr and continue magnesium infusion as 2 gr per hour, thus preventive maternal magnesium levels could be reached and fetal mod-MPI could be investigated.

Conclusions

Magnesium therapy given to preeclamptic or eclamptic women increased fetal mod-MPI significantly, which might show an adverse effect on fetal cardiac function. Neonates born after magnesium therapy might need extra special care.

Author contributions

Hanım Güler Şahin and Gökçe Naz Kucukbas took place in design, planning, data analysis and manuscript writing. Ulku Yaka Kartal took place in data collection, data analysis and manuscript writing.

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Conflict of interest

The authors have no conflicts of interest.

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Figure Legends

Figure 1. Serum magnesium levels before and after magnesium prophylaxis.

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